Docket No. D0287 NP

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**
**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

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| Applicants | : | Riccardo Attar, et al. |
| Application No. | : | 10/620,514 Confirmation No. : 3956 |
| Filed | : | July 16, 2003 |
| For | : | TRANSGENIC NON-HUMAN MAMMALS EXPRESSING A REPORTER NUCLEIC ACID UNDER THE REGULATION OF ANDROGEN RESPONSE ELEMENTS |
| Group Art Unit | : | 1632 |
| Examiner | : | Joanne Hama |

Princeton, New Jersey 08543
November 13, 2006

**Mail Stop Appeal Brief - Patents**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

APPEAL BRIEF

## I. REAL PARTY IN INTEREST

The real party in interest is Bristol-Myers Squibb Company, a corporation organized and existing under the laws of Delaware and having an office and place of business at P.O. Box 4000, Princeton, NJ 08543. The present assignee of this application is Bristol-Myers Squibb Company. 37 C.F.R. § 41.37(c)(1)(i).

## II. RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences known to Appellant or their legal representatives that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal. 37 C.F.R. § 41.37(c)(1)(ii).

## III. STATUS OF CLAIMS

Claims 1-13, 18, and 19, set forth in Appendix A, stand rejected and are on appeal. Claims 14-17 were previously canceled. Claim 20 was canceled in the amendment filed concurrently with this Appeal Brief. 37 C.F.R. § 41.37(c)(1)(iii).

## IV. STATUS OF AMENDMENTS

Claims 1-13 and 18-20 were finally rejected in the June 16, 2006 final Office Action. In their August 15, 2006 Amendment After Final Action, Appellant sought to amend claims 1-4, 7, 11-13, and 20. The Examiner stated in the September 1, 2006 Advisory Action that, for purposes of appeal, the amendments included in Appellant's August 15, 2006 Amendment would be entered. Submitted concurrently with this Appeal Brief is an amendment under 37 C.F.R. § 1.116 that amends claim 18 and cancels claim 20. Therefore, claims 1-13, 18, and 19 should be considered in this Appeal. 37 C.F.R. § 41.37(c)(1)(iv).

## V. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed invention on appeal is directed to certain transgenic mice, certain isolated nucleic acid constructs, and certain methods for obtaining certain transgenic mice.

Independent claim 1 is directed to transgenic mice whose genome comprise a nucleic acid construct that comprises a reporter nucleic acid encoding a reporter operably linked to a promoter comprising an androgen response element (ARE) and an androgen receptor nucleic acid encoding an androgen receptor, wherein expression of the reporter nucleic acid is regulated by expression of the androgen receptor nucleic acid, and wherein the androgen receptor nucleic acid is expressed in the mouse in at least one tissue selected from lung, heart, liver, testis, bone, prostate, and kidney such that the mouse has enhanced expression of androgen receptor relative to a wild type mouse in the at least one tissue. See, *inter alia,* page 5, lines 22-28; page 11, lines 19-25; and page 14, lines 15-21. Claims 2-7, 12, 13, and 18 ultimately depend from claim 1.

Independent claim 8 is directed to isolated nucleic acid constructs that comprise a reporter nucleic acid encoding a reporter operably linked to a promoter comprising an androgen response element (ARE), the constructs further comprising an androgen receptor nucleic acid encoding an androgen receptor, wherein expression of the reporter nucleic acid is regulated by expression of the androgen receptor nucleic acid. See, *inter alia,* page 6, lines 3-9. Claims 9 and 10 depend from claim 8.

Independent claim 11 is directed to methods for obtaining a transgenic mouse whose genome comprises a nucleic acid construct that comprises a reporter nucleic acid encoding a reporter operably linked to a promoter comprising an androgen response element (ARE) and an androgen receptor nucleic acid encoding an androgen receptor, wherein expression of the

reporter nucleic acid is regulated by expression of the androgen receptor nucleic acid, and wherein the androgen receptor nucleic acid is expressed in the mouse in at least one tissue selected from lung, heart, liver, testis, bone, prostate, and kidney, such that the mouse has enhanced expression of androgen receptor relative to a wild type mouse in the at least one tissue, wherein the mouse can be bred to produce progeny mice whose genomes comprise the nucleic acid construct, the method comprising the steps of: (a) isolating a fertilized egg from a first female mouse; (b) transferring a transgene comprising the nucleic acid construct into the fertilized egg; (c) transferring the fertilized egg of step (b) to the uterus of a pseudopregnant second female mouse; and (d) maintaining the second female mouse such that: (i) the second female mouse becomes pregnant with an embryo derived from the fertilized egg of step (c); (ii) the embryo develops into the transgenic mouse; and (iii) the transgenic mouse is viably born from the second female mouse; wherein the genome of the transgenic mouse comprises the nucleic acid construct and wherein the mouse can be bred to produce progeny mice whose genomes comprise the nucleic acid construct. See, *inter alia,* page 6, lines 10-30; page 11, lines 19-25; and page 14, lines 15-21. Claim 19 depends from claim 11.

## VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The following grounds of rejection are to be reviewed on this appeal:

1. Whether claims 1-13, 18, and 19 meet the utility requirement of 35 U.S.C. § 101.

2. Whether one of ordinary skill in the art would know how to use the claimed invention of claims 1-13, 18, and 19 so as to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph.

3. Whether claim 18 is indefinite for lacking antecedent basis under 35 U.S.C. § 112, second paragraph. 37 C.F.R. § 41.37(c)(1)(vi).

## VII. ARGUMENT

### A. The Utility Rejection

#### 1. The Legal Standard for Utility

To meet the utility requirement of 35 U.S.C. §§ 101 and 112, first paragraph, a patent applicant need only show that the claimed invention has "practical utility," *Anderson v. Natta*, 480 F.2d 1392, 1396-97, 178 USPQ 458, 461 (C.C.P.A. 1973) and provides a "specific benefit" to the public. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689, 695 (1966). As discussed by the Federal Circuit in *Juicy Whip Inc. v. Orange Bang Inc.*, 185 F.3d 1364, 1366, 51 USPQ2d 1700, 1702 (Fed. Cir. 1999), this is not a high threshold:

> An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end").

Although an asserted utility must be described with specificity, a patent applicant need not demonstrate utility to a certainty. In *Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 USPQ2d 1094, 1100 (Fed. Cir. 1991), the Federal Circuit explained:

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding lack of utility." *Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984).

An asserted utility is specific if it shows that the claimed invention can be used to provide a well defined and particular benefit to the public. *In re Fisher*, 421 F.3d 1365, 1371, 76 USPQ2d 1225, 12261 (Fed. Cir. 2005). The Utility Guidelines set forth in the MPEP also define a "specific" utility as one that is particular to the subject matter claimed and would not be applicable to a broad class of inventions. MPEP § 2107.01. The "specific" utility requirement is met unless the asserted utility is "so vague as to be meaningless" and amounts to a "nebulous expression" such as "biological activity" or "biological properties" that does not convey meaningful information about the utility of what is being claimed. *See In re Fisher*, 421 F.3d at 1371; *see also Cross v. Iizuka*, 753 F.2d 1040, 1048, 224 USPQ 739, 745 (Fed. Cir. 1985).

If a claimed invention meets at least one stated objective, utility under § 101 is clearly shown. *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 USPQ 592, 598 (Fed. Cir. 1983). Proof of one of the disclosed utilities suffices to meet the statutory utility requirement. *See Standard Oil Co. v. Montedison, S.p.a.*, 664 F.2d 356, 375, 212 USPQ 327, 343 (3d Cir. 1981); *see also Krantz v. Olin*, 356 F.2d 1016, 1019, 148 USPQ 659, 661-62 (C.C.P.A. 1966); *E.I. du Pont de Nemours & Co. v. Berkeley & Co.*, 620 F.2d 1247, 1258 n.10, 205 USPQ 1, 8 n.10 (8th Cir. 1980). Any utility of a claimed compound is sufficient to satisfy 35 U.S.C. § 101. *Cross*, 753 F.2d at 1051, 224 USPQ at 748.

The MPEP sets forth similar guidelines for Examiners. It states that the patent laws only require that applicants establish one specific, substantial and credible utility in order to satisfy the utility requirement, and makes no restrictions on the number of utilities that may be asserted by an applicant:

> It is common and sensible for an applicant to identify several specific utilities for an invention, particularly where the invention is a product (e.g., a machine, an article of manufacture or a composition of matter). However, regardless of the category of invention that is claimed (e.g., product or process), an applicant need only make ***one credible assertion of specific utility*** for the claimed invention to satisfy 35 U.S.C. 101 and 35 U.S.C. 112; ***additional statements of utility, even if not "credible," do not render the claimed invention lacking in utility***. See, e.g., *Raytheon v. Roper*, 724 F.2d 951, 958, 220 USPQ 592, 598 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 835 (1984) ("When a properly claimed invention meets ***at least one stated objective***, utility under 35 U.S.C. 101 is clearly shown."); *In re Gottlieb*, 328 F.2d 1016, 1019, 140 USPQ 665, 668 (C.C.P.A. 1964) ("Having found that the antibiotic is ***useful for some purpose***, it becomes ***unnecessary to decide whether it is in fact useful for the other purposes 'indicated' in the specification as possibly useful.***"); *In re Malachowski*, 530 F.2d 1402, 189 USPQ 432 (C.C.P.A. 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988). Thus, if applicant makes ***one credible assertion*** of utility, utility for the claimed invention as a whole is established.

*See* MPEP § 2107.02 (emphasis added).

In addition to conferring a specific benefit on the public, the benefit must also be "substantial." *Brenner*, 383 U.S. at 534, 148 USPQ at 695. A "substantial" utility is a practical, "real-world" utility. *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881, 883 (C.C.P.A. 1980). Courts have used the labels "practical utility" and "real world" utility interchangeably in determining whether an invention offers a "substantial utility." *In re Fisher*, 421 F.3d at 1371. The C.C.P.A. has stated:

> Practical utility is a shorthand way of attributing "real world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public.

*Nelson*, 626 F. 2d at 856, 206 USPQ at 883. Therefore, to satisfy the "substantial" utility requirement, an applicant must show that the claimed invention has a significant and presently available benefit to the public. *In re Fisher*, 421 F.3d at 1371.

### 2. The Specification Provides A Credible, Specific and Substantial Utility For The Invention of Claims 1-13, 18, and 19

The Examiner has finally rejected claims 1-13, 18, and 19 under 35 U.S.C. § 101 for allegedly lacking utility. The Examiner does not dispute that androgen receptor is an important target in multiple areas of drug discovery and patient therapy, as recited in the specification, *inter alia,* at page 4, lines 4-15. Rather, the Examiner contends that the claimed transgenic mice do not have a phenotype that distinguishes them from wild type mice and, on this basis, concludes that the claimed invention is not supported by a specific utility. Appellant disagrees.

Appellant respectfully submits that the specification, as filed, does indeed establish a credible, specific, and substantial utility for the claimed invention. Independent claims 1 and 11 require that the androgen receptor nucleic acid is expressed in the transgenic mouse in at least one tissue selected from the group consisting of lung, heart, liver, testis, bone, prostate, and kidney, such that the mouse has enhanced expression of androgen receptor relative to a wild type mouse in the at least one tissue. Accordingly, the transgenic mouse of the invention has enhanced expression of androgen receptor relative to wild type mouse in the at least one tissue. The constructs of independent claim 8 can be used to produce the transgenic mice of claims 1 and 11.

As stated in the specification, the transgenic mice of the invention provide a model system to monitor activity of androgen receptor in different organs and tissues. The cells

in which the nucleic acid reporter is expressed can be readily determined by bioluminescence imaging techniques. These transgenic mice are useful for the development of pharmaceutical agents for the treatment of disorders associated with aberrant, up-regulated androgen expression relative to a wild type mouse. In particular, agents can be screened to find those that inhibit or activate the activity of the androgen receptor as measured by the reporter.

The claimed invention has the credible, specific, and substantial use of studying the tissue selective activity of pharmacological agents by inhibition or activation of androgen receptor that is overexpressed in certain tissues. This is not a study of the properties of the transgenic mouse itself but, rather, a study of the ability of an agent to inhibit or activate androgen receptor expression in certain tissues. This use is both credible and specific given that, as is well known in the art and stated in the specification, the androgen receptor is a hormone regulated transcription factor that controls the expression of many genetic programs involved in normal physiological processes as well as in pathological conditions such as cancer. In addition, this is a substantial utility in that it is a real world use (i.e., the identification of androgen receptor modulating agents for the treatment of androgen receptor mediated disorders) rather than studying the properties of the claimed transgenic mouse product itself.

For all of the above reasons, Appellant respectfully submits that the final rejection of claims 1-13, 18, and 19 under 35 U.S.C. § 101 should be reversed.

**B. The Enablement Rejection**

**1. The Legal Standard For Enablement**

To satisfy the enablement requirement under 35 U.S.C.§ 112, first paragraph, the specification must describe how to make and use the claimed invention without undue

experimentation. *See Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916); *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988); *see also* MPEP § 2164. However, a patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986); and *Lindemann Maschinenfabrik GMBH v. Am. Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. § 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (C.C.P.A. 1970). However, failure to disclose other methods by which the claimed invention may be made does not render a claim invalid under 35 U.S.C. § 112. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1533, 3 USPQ2d 1737, 1743 (Fed. Cir. 1987).

If a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard modes of administration are known and contemplated, 35 U.S.C. § 112 is satisfied. *In re Johnson*, 282 F.2d 370, 373, 127 USPQ 216, 219 (C.C.P.A. 1960); *In re Hitchings*, 342 F.2d 80, 87, 144 USPQ 637, 643 (C.C.P.A. 1965). *See also In re Brana,* 51 F.3d at 1566, 34 USPQ2d at 1441.

The Federal Circuit and its predecessor court has made plain that the utility requirement of 35 U.S.C. § 101, and the "how to use" requirement of 35 U.S.C. § 112, first paragraph, have the same basis -- specifically, the disclosure of a credible utility. *In re Brana*,

51 F.3d at 1564 n.12, 34 USPQ2d at 1439 n.12; *In re Jolles*, 628 F.2d at 1326 n.10, 206 USPQ at 889 n.10; *In re Fouche*, 439 F.2d at 1243,169 USPQ at 434.

### 2. The Skilled Worker Would Know How To Use The Invention Of Claims 1-13, 18, and 19

The Examiner has finally rejected claims 1-13, 18, and 19 under 35 U.S.C. § 112, first paragraph stating that since the claimed invention is not supported by either a clear asserted utility or a well-established utility, one skilled in the art would not know how to use the invention. Appellant disagrees.

Appellant respectfully submits that the specification of the instant application discloses to the skilled worker how to make and use the claimed invention. The arguments detailed, *supra,* in Section **A2** concerning the utility of the claimed invention are relevant here. The Federal Circuit and its predecessor court has made plain, the utility requirement of 35 U.S.C. § 101, and the "how to use" requirement of 35 U.S.C. § 112, first paragraph, have the same basis -- specifically, the disclosure of a credible utility. *In re Brana*, 51 F.3d at 1564 n.12, 34 USPQ2d at 1439 n.12; *In re Jolles*, 628 F.2d at 1326 n.10, 206 USPQ at 889 n.10; *In re Fouche*, 439 F.2d at 1243,169 USPQ at 434. And, as discussed above, several credible utilities are disclosed in the application as filed.

Appellant has shown that claims 1-13, 18, and 19 have a specific, substantial and credible utility, as detailed in section **A2**, *supra*. Therefore, the rejection of claims 1-13, 18, and 19 under 35 U.S.C. § 112, first paragraph, cannot stand.

### C. The Indefiniteness Rejection

Claim 18 was rejected under 35 U.S.C. § 112, second paragraph, as lacking antecedent basis. Appellant submits that the amendment to claim 18 submitted concurrently with this Appeal Brief provides antecedent basis for claim 18 dependency to claim 1. Therefore, the rejection of claim 18 under 35 U.S.C. § 112, second paragraph cannot stand.

## VIII. CLAIMS APPENDIX

Appendix A sets forth claims 1-13, 18, and 19 which are pending in this application and are on appeal. 37 C.F.R. § 41.37(1)(c)(viii).

## IX. CONCLUSION

For all of the reasons set forth herein, Appellant respectfully submits that the various rejections of claims 1-13, 18, and 19 are erroneous and requests that the Board overturn them. All of the pending claims should be allowed.

Respectfully submitted,

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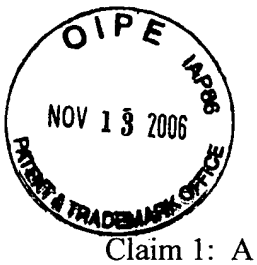


## CLAIMS APPENDIX A

## CLAIMS 1-13, 18, AND 19, ON APPEAL

Claim 1: A transgenic mouse whose genome comprises a nucleic acid construct, wherein said construct comprises a reporter nucleic acid encoding a reporter operably linked to a promoter comprising an androgen response element (ARE), and said construct further comprises an androgen receptor nucleic acid encoding an androgen receptor, wherein expression of said reporter nucleic acid is regulated by expression of said androgen receptor nucleic acid, and wherein said androgen receptor nucleic acid is expressed in said mouse in at least one tissue selected from the group consisting of lung, heart, liver, testis, bone, prostate, and kidney, such that said mouse has enhanced expression of androgen receptor relative to a wild type mouse in said at least one tissue.

Claim 2: The transgenic mouse of claim 1 wherein said reporter is luciferase.

Claim 3: The transgenic mouse of claim 1 wherein said androgen response element is 2XDR-1.

Claim 4: A cell isolated from the transgenic mouse of claim 1, wherein the genome of said cell comprises said nucleic acid construct.

Claim 5: The cell of claim 4 wherein said reporter is luciferase.

Claim 6: The cell of claim 4 wherein said androgen response element is 2XDR-1.

Claim 7: A cell line comprising the cell of claim 4.

Claim 8: An isolated nucleic acid construct that comprises a reporter nucleic acid encoding a reporter operably linked to a promoter comprising an androgen response element (ARE), and said construct further comprises an androgen receptor nucleic acid encoding an androgen receptor, and wherein expression of said reporter nucleic acid is regulated by expression of said androgen receptor nucleic acid.

Claim 9: The construct of claim 8 wherein said reporter is luciferase.

Claim 10: The construct of claim 8 wherein said androgen response element is 2XDR-1.

Claim 11: A method for obtaining a transgenic mouse whose genome comprises a nucleic acid construct, wherein said construct comprises a reporter nucleic acid encoding a reporter operably linked to a promoter comprising an androgen response element (ARE), and

said construct further comprises an androgen receptor nucleic acid encoding an androgen receptor, wherein expression of said reporter nucleic acid is regulated by expression of said androgen receptor nucleic acid, and wherein said androgen receptor nucleic acid is expressed in said mouse in at least one tissue selected from the group consisting of lung, heart, liver, testis, bone, prostate, and kidney, such that said mouse has enhanced expression of androgen receptor relative to a wild type mouse in said at least one tissue,

wherein said mouse can be bred to produce progeny mice whose genomes comprise said nucleic acid construct, said method comprising the steps of:

(a) isolating a fertilized egg from a first female mouse;

(b) transferring a transgene comprising said nucleic acid construct into the fertilized egg;

(c) transferring the fertilized egg of step (b) to the uterus of a pseudopregnant second female mouse; and

(d) maintaining said second female mouse such that:

(i) said second female mouse becomes pregnant with an embryo derived from said fertilized egg of step (c);

(ii) said embryo develops into said transgenic mouse; and

(iii) said transgenic mouse is viably born from said second female mouse;

wherein the genome of said transgenic mouse comprises said nucleic acid construct and wherein said mouse can be bred to produce progeny mice whose genomes comprise said nucleic acid construct.

Claim 12: A method for producing a transgenic mouse cell line that expresses a reporter nucleic acid, said method comprising:

(a) isolating cells from the transgenic mouse of claim 1; and

(b) placing the isolated cells under conditions to maintain growth and viability of the isolated cells such that said transgenic mouse cell line expresses said reporter nucleic acid.

Claim 13: A method of screening for a modulator of the androgen receptor, comprising administering a test substance to the transgenic mouse of claim 1 and assaying the effect of said test substance on the activity of the androgen receptor.

Claim 18: The transgenic mouse of claim 1 wherein said nucleic acid construct comprises SEQ ID NO:1.

Claim 19: The method of claim 11 wherein said nucleic acid construct comprises SEQ ID NO:1.

## EVIDENCE APPENDIX B

**NONE**

# RELATED PROCEEDINGS APPENDIX C

**NONE**